

## Association between hsCRP Levels, Glycemic Control and Total Interatrial Conduction Time in Patients with Type 2 Diabetes Mellitus

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### ABSTRACT

**Background:** Type 2 Diabetes Mellitus (T2DM) represents one of the most important risk factors for atrial fibrillation (AF). Numerous studies have shown that T2DM and poor glycemic control reflected by glycated hemoglobin A1c (HbA1c) levels are independently associated with new onset AF. Recent experimental studies reported that the increased susceptibility to AF in the diabetic patients was presumably due to the slowing of conduction associated with increased interstitial fibrosis. Systemic inflammation can play role in the development of atrial fibrillation. High-sensitivity C-reactive protein (hsCRP) is an inflammatory biomarker that independently predicts the cardiovascular risk. This study aimed to determine the association between hsCRP level and glycemic control with total interatrial conduction time in T2DM patients.

**Subjects and Method:** This was an observational analytic study with cross-sectional design. A total of samples were 41 patients with T2DM. Peripheral venous blood samples to measure hsCRP and HbA1c were drawn in all study population. The total interatrial conduction time was measured by tissue Doppler echocardiography. Multivariate analysis was performed using multiple regression analysis.  $p < 0.050$  was considered to indicate a statistically significant difference.

**Results:** The high-sensitivity C-reactive protein level was higher in the T2DM patients with  $\text{HbA1c} \geq 7\%$  than in the T2DM patients with  $\text{HbA1c} < 7\%$ , but not statistically significant ( $0.44 \pm 0.30$  vs  $0.32 \pm 0.22$ ;  $p = 0.183$ ). The total atrial conduction time was longer in the T2DM patients with  $\text{HbA1c} \geq 7\%$  than in T2DM patients with  $\text{HbA1c} < 7\%$ , but not statistically significant ( $100.29 \pm 28.53$  vs  $94.88 \pm 16.50$ ;  $p = 0.449$ ). Multiple regression analysis showed that hsCRP levels and glycemic control had significant positive correlation with total interatrial conduction time in T2DM patients ( $r = 0.51$ ;  $p = 0.004$ ).

**Conclusion:** The hsCRP levels and glycemic control were significant positively correlated with total interatrium conduction time in patients with type 2 diabetes.

**Keywords:** hsCRP, glycemic control, HbA1c, total interatrial conduction time

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### BACKGROUND

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Diabetes mellitus (DM) and cardiovascular disease often appear as two sides of a coin. DM is considered equivalent to coronary heart disease (Maqri and Fava, 2012). As a consequence, the mortality and incidence of all forms of cardiovascular disease in people with higher DM two to eight times higher than in people without diabetes are risk factors for arrhythmia. The risk factors

which act as arrhythmogenic substrate in patients with diabetes involves the autonomic nervous system disorders, ischemia, conduction time interatrium elongation, heterogeneous repolarization in the atria and ventricles, myocardial damage and scar formation (Nakou et al., 2012).

Based on a meta-analysis study, the current risk of atrial fibrillation increased significantly in diabetic patients (Zhang et al., 2014). DM is a risk factor independent

of atrial fibrillation (Watanabe et al., 2012). Study Framingham Heart Study states that diabetes is proven as a cause of new-onset atrial fibrillation in a cohort study of men and women who were followed for 38 years (OR 1.4 for men and 1.6 for women) (Nakou et al., 2012). Study recent meta-analysis indicate that individuals with diabetes have a risk of > 40% to occur atrial fibrillation than individuals without diabetes (Liu et al., 2012). This risk will increase the longer duration of diabetes and the poor glycemic control (Dublin et al., 2010). Atrial fibrillation is a marker of poor prognosis in patients with DM (Lin et al., 2013). Atrial fibrillation risk > 60% of all causes of mortality and have a higher risk to cardiovascular death, stroke, and heart failure. However, the contribution of diabetes on the prevalence and incidence of atrial fibrillation still requires a variety of advanced study (Goudis et al., 2015).

The atrial fibrillation pathophysiology in patients with diabetic is not known yet (Liu et al., 2012; Yazici et al., 2007). The presence of arrhythmogenic atrial remodeling is expected to have an important role in the pathophysiology of atrial fibrillation in patients with diabetes. Arrhythmogenic atrial remodeling is defined as the change in the structure and function of the atria that can trigger atrial arrhythmias such as atrial fibrillation (Nattel and Harada, 2014). Pathophysiology of atrial fibrillation in diabetes include: remodeling autonomous systems, electrical, electromechanical, and anatomy due to oxidative stress, remodeling up my, and fluctuations in blood sugar (Goudis et al., 2015). Remodeling anatomy can be a major substrate of atrial fibrillation occurrence in diabetes (Liu et al., 2014). The substrate of atrial fibrillation is the electrical function abnormalities in atrial tissue itself (Quintana et al., 2012). Study Kato et al (2008) reported a inter-

atrium conduction disturbances due to atrial interstitial fibrosis which can be a key substrate initiation of atrial fibrillation. Hyperglycemia cause atrial dilatation and interstitial fibrosis, as well as electrical remodeling re-sulting in a prolongation of the conduction time interatrium and increased susceptibility to atrial fibrillation (Liu et al, 2014).

Changes in the form of electrical systems in the form of shortening atrial refractory period of the atrium and sinus impulse propagation is not homogeneous the electrophysiological characteristics that tend to cause atrial fibrillation (Bakirci et al., 2015). Shortening of the atrial refractory period and propagation of sinus impulses are not homogeneous cause prolongation of the conduction time interatrium. As a result there is a delay between electrical activation of the mechanical contraction that atrial electromechanical function impaired (Goudis et al., 2015). Interatrial conduction time total reflects atrial electromechanical function and can be used as a marker of atrial remodeling remodeling both electric and anatomy (Uijl et al., 2011; Deniz et al., 2012). Elongation interatrium conduction time is closely related to the mechanisms underlying abnormalities in the atrium directly or indirectly, and one of the conditions for the initiation and development of atrial fibrillation (Weijs et al., 2011). Elongation interatrium total conduction time has been proven to increase the risk of atrial fibrillation in many studies (Antoni et al., 2010). Various different methods can be used to evaluate the total interatrium conduction time. Although electrocardiography and echo cardiography examination is used to measure the conduction time interatrium, cardiac electrophysiology examination is still the gold standard examination (Merckx et al., 2005). Currently, echo-cardiography with dopler networks are often

used to measure the conduction time interatrium in various studies. Although it is not the gold standard examination, this examination is preferred to measure conduction time interatrium because it is non-invasive and the results are believed to correspond to the examination of cardiac electrophysiology (Fatma et al., 2015). Previous study indicates total elongation conduction time interatrium a strong predictor of the incidence of atrial fibrillation (Weijs et al., 2011).

Various data also showed that the longer the duration of diabetes or for worse glycemic control, also increase the risk of atrial fibrillation (Dublin et al., 2010). Study Dublin et al., (2010) reported that there is a significant correlation between HbA1C levels with risk of atrial fibrillation. The study showed that each increase by 1% in HbA1c levels associated with an increased relative risk of atrial fibrillation 1:14 (95% CI= 0.96 to 1:35). Therefore, there is a free relationship between DM and poor HbA1c levels with an increased risk of atrial fibrillation. However, the contribution of diabetes on the prevalence and incidence of atrial fibrillation is based on glycemic control still needs further studies (Zhang et al., 2014).

DM has been associated with the production of excessive reactive oxygen species and decreased antioxidant capacity, resulting in tissue damage (Stadler, 2012). Various studies have also reported that inflammation and oxidativestress play a role in atrial electrical remodeling anatomy and thus plays an important role in the formation and development of atrial fibrillation (Ozaydin 2010; Korantzopoulos et al., 2007; Rudolph et al., 2010). Inflammation and oxidative stress is thought to be one cause of atrial interstitial fibrosis and atrial electromechanical function disorders, thereby facilitating the occurrence and de-

velopment of atrial fibrillation (Fu et al., 2013; Liu and Li, 2008). Systemic inflammation in diabetes increases levels of C-reactive protein (CRP) that predispose occur atrial fibrillation. Local activation of the complement system mediated by binding of CRP with phospholipid components of damaged cells (Antonio, 2006). Examination of high-sensitivity C-reactive protein (hsCRP) is a marker of systemic inflammation and tissue damage that can predict the risk of cardiovascular disease (Antonio, 2006). Various studies also showed elevated levels of hsCRP be a strong predictor of atrial fibrillation (Galea et al., 2014). However, there has been no considerable literature on the relationship of atrial fibrillation with inflammation in diabetic patients (Bakirci et al., 2015).

Currently, there are no studies on the effect of inflammation on interatrial conduction time total which is a predictor of early development of atrial fibrillation in patients with type 2 diabetes based on glycemic control. Therefore, the authors wanted to examine a possible relationship between hsCRP levels and glycemic control with total interatrium conduction time in patients with type 2 diabetes.

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## SUBJECTS AND METHOD

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This was an analytic-observational study with cross sectional design. It was conducted on April 2016 in the installation of the Outpatients Clinic of Internal Medicine at Dr. Moewardi Hospital, Surakarta. There were forty one patients with type 2 diabetes mellitus selected for this study. The inclusion criteria were patients aged >18 years with sinus rhythm based on the examination of electrocardiography (ECG). The exclusion criteria in this study were malignancy, liver cirrhosis, immunological disease (both immunodeficiency diseases

and auto-immune), systemic infection (by clinical examination, white blood cell count  $> 12 \times 10^9/\text{mL}$ , or a temperature  $> 37.5^\circ\text{C}$ ), and the use of drugs and non-steroidal anti-inflammatory steroid 1 last month.

Echocardiography performed using GE Vivid S6. During echocardiography, patients underwent ECG recording. Doppler Tissue Imaging (TDI) examination measured the total interatrial conduction time (Interval PA-TDI). PA-TDI interval defined as the time interval from the initiation of the P wave in electrocardiography recorded on echocardiographic tool (lead II) until the crest of the wave A in the picture Doppler atrial tissue which measured three times of cardiac cycle and averaged. Abnormality measurements performed such as stenosis or regurgitation of heart valves, segmental analysis, the existence of anatomical abnormalities, the dimensions of heart chambers, left ventricular function.

HsCRP examination performed before or after the echocardiographic data retrieval. HsCRP blood samples were taken from the antecubital vein processing. It conducted at the Laboratory of Clinical Pathology, Dr. Moewardi Hospital. HsCRP examination was using Latex immunoturbidimetry on ADVIA 1800 Chemistry Syste (Siemens Healthcare Diagnostic, Deerfield, IL).

Multiple linear regression analysis was used to analyze the relationship between hsCRP and glycemic control (HbA1c levels) with a total interatrial conduction time with the following formula:

$Y$  = interatrium total conduction time (continuous data)

$X_1$  = hsCRP (continuous data)

$X_2$  = glycemic control based on HbA1c (categorical data)

$\beta_0, \beta_1, \beta_2$  = coefficient regression

The correlation coefficient ( $r$ ) indicates how the relationship between hsCRP

levels and glycemic control simultaneously the conduction time interatrial total.  $R$  ranges from 0 to 1 means that the relationship is getting stronger. Guidelines to provide interpretation of correlation coefficient as follows:

to 0.199 = very low

0.20 to 0.399 = low

0.40 to 0.599 = moderate

0.60 to 0.799 = strong

0.80 to 1.000 = very strong

The coefficient of determination ( $R^2$ ) is the coefficient used to determine how much hsCRP and glycemic control affects the conduction time interatrial total. This coefficient shows how much percentage of variation of hsCRP and glycemic control was able to explain the variation in total interatrial conduction time. The  $p$ -value  $< 0.050$  states the difference statistically significant. Data analysis measured using SPSS (version 22.0; SPSS Inc., Chicago, IL, USA).

## RESULTS

Subject of the study consisted of 17 patients with type 2 diabetes with HbA1c  $< 7\%$  (mean age  $63.12 \pm 9.38$  years; 22.7% men) and 24 patients with type 2 diabetes with HbA1c  $\geq 7\%$  (mean age  $58.33 \pm 9.41$  years; 11.4% men). From Table 1 the characteristics of the subjects with well-controlled blood sugar (HbA1c  $< 7\%$ ) and poorly controlled blood sugar (HbA1c  $\geq 7\%$ ) did not differ significantly ( $p > 0.050$ ). Type 2 diabetes patients with HbA1c  $\geq 7\%$  had higher hsCRP levels compared to patients with type 2 diabetes with HbA1c  $< 7\%$ , but not statistically significant ( $0.44 \pm 0.30$  versus  $0.32 \pm 0.22$ ;  $p = 0.183$ ).

**Tabel 1. Characteristic of clinic and laboratory data in DM type 2**

	HbA1c <7% (n = 17)	HbA1c ≥7% (n = 24)	p
Age, Year	63.12 ± 9.38	58.33 ± 9.41	0.117
Gender, male (%)	22.7	11.4	0.200
BMI (kg/m <sup>2</sup> )	24.56 ± 4.30	25.73 ± 3.91	0.378
Smoking (%)	6.8	18.2	0.157
Blood pressure (mmHg)			0.059
<140/90	18.2	15.9	
≥140/90	20.5	38.6	
Pulse rate (Pulse/minute)	82.00 ± 8.00	79.29 ± 11.83	0.387
Illness duration (%)			0.317
< 5 years	18.2	11.4	
5-10 years	15.9	27.3	
≥ 10 years	4.5	15.9	
Coronary heart disease (%)	4.5	11.4	0.414
Valvular heart disease (%)	9.1	6.8	0.655
hsCRP (mg/L)	0.32 ± 0.22	0.44 ± 0.30	0.183
<i>Glycated Haemoglobin (HbA1c); Body Mass Index (BMI); Systolic Blood Pressure(SBP); Diastolic Blood Pressure (DBP); high sensitivity C-reactive protein (hsCRP).</i>			

**Table 2. Characteristics of echocardiography in subjects with type 2 Diabetes**

	Hba1c <7% (N = 17)	Hba1c ≥7% (N = 24)	p
Left Ventricular Ejection Fraction (%)	65.71 ± 10.13	59.33 ± 15.87	0.125
Left Atrial Diameter (Mm)	31.65 ± 5.88	31.29 ± 5.66	0.848
Ratio E/A	0.78 ± 0.21	0.92 ± 0.49	0.272
Ratio Em/Am	0.85 ± 0.31	0.83 ± 0.32	0.827
Ratio E/Em	7.08 ± 2.97	8.46 ± 3.96	0.210
Total of interatrial conduction time (Ms)	94.88 ± 16.50	100.29 ± 28.53	0.449
<i>E, Mitral Annular Early Diastolic Velocity; A, Mitral Annular Late Diastolic Velocity; Em, Tissue Doppler Mitral Annular Early Diastolic Velocity; Am, Tissue Doppler Mitral Annular Late Diastolic Velocity; Mm, Millimeter; Ms, Miliseconds.</i>			

**Table 3. The results of multiple linear regression analysis of the association between hsCRP levels and glycemic control (HbA1c) with a total interatrial conduction time in patients with type 2 Diabetes Mellitus.**

Variables	β	95% CI		p
		Lower	Upper	
Contants	77.54	64.19	90.89	<0.001
hsCRP (mg/dL)	38.78	14.01	63.54	0.003
HbA1c ≥7%	14.04	0.09	27.98	0.048
N observation= 41 subjects				
Correlation Coefficient (R)= 0.51				
Determination Coefficient (R <sup>2</sup> )= 21.6%				
p = 0.004				

In Table 2 echocardiographic characteristics of subjects with well-controlled blood glucose (HbA1c<7%) and poorly controlled blood sugar (HbA1c≥7%) did not differ significantly (p>0.050). Total atrial conduction time in patients with type 2

diabetes with HbA1c ≥ 7% longer compared with patients with type 2.

Diabetes with HbA1c <7%, but not statistically significant (100.29 ± 28.53 versus 94.88 ± 16.50; p= 0.449). Multiple regression analysis was conducted to determine whether there is a relationship bet-

ween hsCRP levels and glycemic control with total interatrial conduction time in patients in this study.

Based on the results, it appears that there is a moderate correlation between hsCRP levels and glycemic control with a total interatrial conduction time. The coefficient of determination shows that percentage contribution and influence of glycemic control hsCRP the conduction time interatrial 21.6%. Seventy eight percent influenced other variables not included in this study. The equation was found that each increase of hsCRP then interatrial total conduction time of 38.78 milliseconds. In HbA1c  $\geq 7\%$  the total interatrial conduction time would be increase of 14.04 milliseconds ( $p=0.004$ ). It shows that the obtained results were statistically significant.

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## DISCUSSION

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This study showed that hsCRP levels and glycemic control (HbA1c) correlated positive with the total interatrial conduction time in patients with type 2 diabetes. Epidemiological studies have shown that the incidence of atrial fibrillation was higher in patients with type 2 diabetes compared with normal subjects (Johansen et al., 2008). Atrial fibrillation is the most common cardiac arrhythmia that increased morbidity and mortality, including stroke, heart failure, and decreased quality of life (Voigt and Dobrev, 2012; Yuniadi et al., 2014). Patients with atrial fibrillation at risk of stroke five times and heart failure three times higher than the patients without atrial fibrillation (Yuniadi et al., 2014).

Currently, the number of patients with atrial fibrillation increase, so the primary prevention of the new onset atrial fibrillation important to do. Primary pre-

vention strategies can be done if the clinician is able to identify patients at high risk for the occurrence of atrial fibrillation (Vos et al, 2009). Pathophysiology that cause diabetes predispose to atrial fibrillation include ventricular hypertrophy, ischemia/ fibrosis of the myocardium, remodeling of the left atrium, impaired autonomic tone and inflammation (Liu et al, 2009). Hayden et al., (2006) showed that high blood glucose levels can induce myocardial fibrosis in rats. In addition, patients with diabetes higher levels of C-reactive higher protein, a marker systemic inflammation, which lead to myocardial fibrosis and diastolic dysfunction (Yuan et al, 2006). The risk coronary heart disease and heart failure was higher in patients with diabetes increased the incidence of atrial fibrillation (Dublin et al, 2010).

This study demonstrated a positive linear relationship between HbA1c levels with a total of interatrial conduction time, where HbA1c  $\geq 7\%$  the total of interatrial conduction time would increase of 14.04 milliseconds. Risk of atrial fibrillation in patients with diabetes is associated with glycemic control (Fatemi et al., 2014).

Huxley et al., (2012) showed a positive linear relationship between HbA1c with risk of atrial fibrillation in diabetic patients with an odds ratio of 1.13 per 1% increase in HbA1c levels. Therefore, diabetes and poor glycemic control, as measured by A1C, associated with an increased risk of atrial fibrillation. Interatrial total conduction time measured by echocardiography doppler network (PA-TDI). It reflects atrial activation that used to detect atrial electro-mechanical interference (Hata et al, 2014). Remodeling atrium can be detected from presence of atrial conduction disturbance and dispersion of atrial refractory period, which trigger reentry process and the onset of atrial fibrillation (Bakirci et al., 2015).

Interatrial total conduction time is the time from initiation to the end of the atrial depolarization activation of the same place. Elongation conduction time interatrium total reflecting decreased conduction velocity and atrial dilatation can be a substrate for the occurrence of atrial fibrillation (Heijman et al., 2014). Decrease in conduction velocity cause shortening circuit or path of action potential depolarization and occur repeatedly, causing micro reentry (multiple wavelet reentry). Reentry mechanism is one of the occurrence of atrial fibrillation (Represents et al., 2011). So, the measurement of total interatrial conduction time can be used as predictor of incident atrial fibrillation (Ozlu et al., 2013; Vos et al., 2009).

Vos et al., (2009) showed that the total interatrial conduction time is short (<130 milliseconds) can prevent patients from atrial fibrillation events. So clinicians can consider this patient is not a candidate to do primary prevention of the occurrence of atrial fibrillation. Patients with conduction time interatrial total >165 milliseconds at risk for atrial fibrillation occurs and may be a candidate for the primary prevention of the occurrence of atrial fibrillation using cardiovascular drugs. Patients with conduction time interatrial total >190 milliseconds very risky to occur atrial fibrillation. These patients can be treated with anticoagulants prophylactically, especially if the patient has a score CHADS<sub>2</sub> (congestive heart failure, hypertension, age = 75 years, diabetes mellitus, stroke) is high (Vos et al., 2009). CHADS<sub>2</sub> score is used to predict the risk of stroke in patients with atrial fibrillation non valves (Lane and Lip, 2012).

Liu et al (2012) showed that atrial electromechanical function disorders associated with increased total interatrium conduction time. Kato et al., (2006) showed

interatrial conduction time delays and increased deposition of fibrotic atrium plays an important role in the incidence of atrial arrhythmogenic. This indicates that the structure of atrial remodeling characterized by interstitial fibrosis may be one of the main mechanisms of the occurrence of atrial fibrillation in DM (Kato et al., 2006). Fu et al., (2013) detected conduction time interatrial total lengthwise on rabbit diabetes than the control group. But certainly elongation pathophysiology interatrial conduction time in patients with diabetes is still unknown. This study shows that there is a positive correlation between the hsCRP with intreatrial conduction time. Interatrial conduction time would be increased of 38.78 milliseconds in every unit of hsCRP unit increased. Histological examination showed infiltrates of inflammatory and oxidative damage to the atrial tissue in patients with atrial fibrillation (Boss et al., 2006). Liu et al, 2008) showed that inflammation is one of the mechanisms of atrial fibrillation in patients with diabetes. Inflammatory stimulus triggering fibroblast proliferation, migration, and transformation also miofibroblas causes atrial remodeling characterized by shortening of atrial refractory period (Friederichs et al., 2011). Various studies have observed the relationship of inflammation in atrial fibrillation with inflammatory markers such as CRP, hsCRP, and interleukin (IL) -6 (Boos et al., 2006). Bakirci et al (2015) demonstrated total conduction time interatrium positively correlated with CRP levels in patients with type 2 diabetes mellitus. Oxidative stress and inflammation are also a key component and is associated with poor glycemic control, the pathogenesis of diabetes and its complications (Gohel and Chacko, 2013). Sarinnapakorn et al., (2013) showed levels of hsCRP were positively correlated with HbA<sub>1c</sub> levels where the

mean HbA1c levels were significantly higher in patients with hsCRP levels  $\geq 1$  mg / L. Other factors such as age, blood pressure, body mass index, LDL cholesterol, serum creatinine did not correlate with levels of hsCRP (Sarinnapakorn et al., 2013). Bahceci et al (2005) showed no significant difference in hsCRP levels in patients with type 2 diabetes without coronary heart disease in patients with non-type 2 diabetes have coronary heart disease. But type 2 diabetes patients who had coronary artery disease have higher levels of hsCRP than patients with non-type 2 diabetes and coronary heart disease (Bahceci et al., 2006). Therefore, oxidative stress and inflammatory markers can be used as an additional examination in addition to HbA1c to assess cardiovascular risk in diabetic patients with poor glycemic control (Dilshad and Shazia, 2009).

In addition to glycemic control, cardiovascular risk factors such as dyslipidemia, hypertension, smoking, and obesity may influence the inflammatory status of individuals (Montori, 2008). HsCRP levels in this study had a fairly large standard deviation in both subjects with well-controlled blood glucose and poorly controlled ( $0.32 \pm 0.22$  versus  $0.44 \pm 0.30$ ). This indicates blood glucose control alone cannot be used to determine the status of inflammation.

Based on multivariate analysis, hsCRP levels and glycemic control correlated (positively) moderate ( $OR=0.51$ ;  $p=0.004$ ) with total interatrial conduction time. Studyrs simply observe the relationship of inflammation and glycemic control with total interatrial conduction time. However, a variety of other causes, such as cardiac remodeling autonomous system, activation of the renin angiotensin aldosterone system, sympathetic over activity, changes in fibrosis due to hyperglycemia, all of

which may lead to an increase in the frequency of atrial fibrillation and the deterioration of the function of the left atrium, can cause prolongation of the conduction time interatrium total. Hypertension, a history of paroxysmal atrial fibrillation, heart valve abnormalities, increasingly older age and body mass index were higher also can prolong the conduction time interatrial total (Weijs et al., 2011).

Characteristics of the subjects with poorly controlled blood glucose have a body mass index higher, more hypertension, and diabetes duration longer than subjects with well-controlled blood sugar. This study shows the percentage contribution of the influence of hsCRP and glycemic control of the conduction time interatrial 21.6%. While the rest of 78.4% may be affected by other variables such as body mass index, hypertension, duration of diabetes, and a history of paroxysmal atrial fibrillation.

Various echocardiographic parameters can be correlated with total interatrial conduction time. The increase in left atrial dimension, increasing the diameter of the aortic, mitral and aortic regurgitation and diastolic dysfunction associated with prolongation of the conduction time interatrial total. Mild diastolic dysfunction may be a sign of ventricular relaxation disorders. The increase in left atrial dimension may reflect an increase in left atrial pressure that can occur in left ventricular diastolic dysfunction (Weijs et al., 2011).

However, the validation study demonstrated an electromechanical process is constant. In addition, the slightest delay time when the ECG processing occurs on all machines echocardiography. However, this delay is consistent so it should not interfere with the results of this study. Other researcher also cannot detect paroxysmal atrial fibrillation episodes that may have occurred on the subject of study, because they do an



EKG only one time of the study. Furthermore, diabetic neuropathy which is not visible can mask the symptoms of atrial fibrillation-related heart.

Echocardiography measurement convenient form of measurement conduction time interatrial total help identify patients with type 2 diabetes (especially those that have the status of glycemic control was bad and elevated levels of hsCRP). A risk of atrial fibrillation, so primary prevention can be done more effectively by reducing the number of patients treated (number needed to treat). However, these results need to be validated with a cohort study to strengthen the scientific evidence.

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